REMARKS

Claims 106-110 and 112-121 are pending in the application. In the present amendment, claims 93-105 and 111 are canceled without prejudice to pursuing any canceled subject matter in this or another application. Claim 106 is amended to recite a particular vesicular composition, and claims 116 and 119 are amended for clarity and consistency with claim 106. Claim 121 is added. No new matter has been added by this amendment, as support is found throughout the specification, for example, at page 11, lines 8-12; page 18, lines 9-12 and 16-26; page 19, lines 1-4; page 26, lines 21-24; page 27, lines 1-3; page 42, as-filed claim 1; and page 43, as filed claim 7.

Rejection Under 35 U.S.C. §112, first paragraph

Claims 93-120 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement due to the use of "consisting essentially of" in the independent claims. The Office Action asserts that the application does not include sufficient support for this term as applied to non-steroidal anti-inflammatory drugs (NSAIDs).

The Office Action does not identify any case law or other authority requiring strict word-for-word support for claim language, such as the transitional phrase "consisting essentially of." To the contrary, in outlining the requirement that a claim as a whole, including a transitional phrase, must be sufficiently supported to satisfy the written description requirement, MPEP § 2163(I), entitled "General Principles Governing Compliance with the 'Written Description' Requirement for Applications," cites *Lockwood v. Am. Airlines Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997), to show that an applicant shows possession of a claimed invention "by such descriptive means as words . . . that fully set forth the claimed invention." *Lockwood* goes on to state that "the exact terms need not be used *in haec verba*," *id.*, but that "the specification must contain an equivalent description of the claimed subject matter," *id.* Furthermore, the Federal Circuit has stated that a patentee can "define[] the scope of the phrase 'consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention." *PPG Indus. Inc. v. Guardian Indus. Corp.*, 156 F.3d 1351, 1355 (Fed. Cir. 1998).

With respect to the pending claims reciting vesicles consisting essentially of one or more phosphatidyl cholines, a salt of one or more NSAIDs and one or more stabilizers (claim 106), and further consisting essentially of one or more consistency modifiers and/or antioxidants (claim 116), the specification describes vesicles or transfersomes including two components having different solubilities (*e.g.*, page 6, line 14, to page 7, line 11). At page 18, line 16-19, the specification states that "[a]s less polar components, inventive preparations may contain a physiologically compatible lipid, preferably from the class of phospholipids and especially from the class of phosphatidyl cholines, the active ingredient, for example, ibuprofen, diclofenac or a salt thereof, being the more soluble component . . . ." The following paragraph, at page 19, lines 1-4, states further that "[i]nventive preparations additionally may comprise consistency modifiers, such as hydrogels, antioxidants such as probucol, tocopherol, BHT, ascorbic acid, desferroxamine and/or stabilizers such as phenol, cresol, benzyl alcohol, etc." Thus, these paragraphs provide support for a vesicle "consisting essentially of" the components identified in claims 106 and 116 as amended herein.

Furthermore, the specification provides sufficient written description that one skilled in the art could determine what constitutes a material change in the basic and novel characteristics of the claimed vesicles. For example, page 6, lines 19-24, states "the carrier substance compris[es] at least two amphiphilic components, which are physically and/or chemically different and differ in their solubility in the suspension medium of the transfersomes (usually water), by a factor of at least 10, if their content of solubilizing components amounts to less than 0.1 mole percent based on the content of these substances . . . ." Page 7, lines 3-11, states "the solubilities of the individual carrier components of the transfersome in the suspension medium differ at least by a factor of 10 (and of up to 10^7)." At page 19, line 8, to page 23, line 9, the application describes the "principle of action" of vesicles as claimed, and identifies criteria that allow the vesicles to provide for the transport of an active ingredient, such as an NSAID, through skin or mucous membranes as claimed. Page 10, line 15, to page 11, line 2; page 22, line 3, to page 23, line 9; and page 29, lines 3-5, indicate how certain characteristics of the vesicles can be determined, and such methods are also illustrated in the Examples.

In sum, "consisting essentially of" as applied to NSAIDs in the pending claims is supported in the specification, and can be defined with reference to passages in the specification describing vesicle function and evaluated using described methods. Accordingly, it is believed

that the specification fully supports the pending claims' consisting-essentially-of language, and it is respectfully requested that the present § 112, first paragraph rejection, be withdrawn.

Rejections Under 35 U.S.C. §112, second paragraph

Claims 93-120 were rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite due to the recitation of "non-steroidal anti-inflammatory drug *surfactants*" in claim 93.

Without acquiescing in the propriety of the rejection, claim 93 has been canceled without prejudice, and the pending claims do not recite "surfactants." Thus, it is believed that this rejection has been overcome.

Claim 111 was rejected as being allegedly indefinite for reciting percutaneous or oral or parenteral administration, when it depends from claim 106 reciting transporting an NSAID through skin or mucous membranes. Claim 111 has been canceled without prejudice.

Accordingly, the it is believed that the pending claims are clear and definite, and it is respectfully requested that the present § 112, second paragraph, rejections be withdrawn.

Rejections Under 35 U.S.C. §102

Claims 93-97, 100-103, 106-111 and 114-117 have been rejected under 35 U.S.C. § 102(e) as being allegedly anticipated by U.S. Patent No. 5,763,422 to Lichtenberger *et al.* ("Lichtenberger").

Claims 93-95, 98-103, 106, 107, and 111-117 have been rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by U.S. Patent No. 4,369,182 to Ghyczy *et al.* ("Ghyczy").

Claims 93-99, 102-104, 106-113 and 116-118 have been rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Hayward *et al.* ("Hayward").

None of the cited references anticipates the pending claims, because none of the references discloses a method including every element of independent claim 106, in particular, a method for transporting an NSAID through the skin or mucous membrane, comprising administering a vesicle that consists essentially of one or more phosphatidyl cholines, a salt of one or more NSAIDs, and one or more stabilizers.

Neither Lichtenberger, Ghyczy nor Hayward discloses vesicles comprising, much less consisting essentially of, one or more stabilizers (see office action, page 6, item 14, lines 4 and 5). Thus, none of the cited references discloses every element of independent claim 106.

Accordingly, the pending claims are not anticipated by the cited references. Therefore, it is believed that the present § 102 rejections cannot stand and should be withdrawn.

Rejections Under 35 U.S.C. §103(a)

Claims 98, 99, 112 and 113 have been rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Lichtenberger.

Claims 96, 97 and 108-110 have been rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Ghyczy.

Claims 100, 114 and 120 have been rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Hayward alone or in combination with Lichtenberger or Ghyczy.

Claims 104, 105, 118 and 119 have been rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Lichtenberger, Ghyczy or Hayward in combination with U.S. Patent No. 5,209,720 to Unger ("Unger").

The Office Action states that Lichtenberger, Ghyczy and Hayward do not disclose the use of antioxidants and stabilizers, but cites Unger as disclosing these elements.

Unger discloses methods for inducing ultrasonic hyperthermia, comprising intravascularly, intralymphatically, parenterally, subcutaneously, intramuscularly, intraperitoneally, interstitially, hyperbarically, orally or intratumorly administering gas-filled liposomes to tissue or fluid and exposing the tissue or fluid to ultrasound (Abstract; col. 1, line 65, to col. 2, line 12; col. 9, lines 22-26). Unger states "[b]y using the potentiators of the present invention, hyperthermic ultrasound becomes a better, more selective and more effective therapeutic method for the treatment of tumors, inflammation, and arthritis" (col. 2, lines 13-17). Unger does not disclose a vesicle consisting essentially of, *inter alia*, a salt of one or more NSAIDs.

Also in contrast to Unger, the presently claimed methods comprise administering *to the skin* of a human or an animal a vesicle consisting essentially of, *inter alia*, a salt of one or more NSAIDs. Unger in concerned with generating hyperthermia in tissue or fluid; the presently claimed methods relate to transporting an NSAID through skin or mucous membranes. Unger's methods require ultrasound for generating a therapeutic effect; the presently claimed methods do not. The liposomes of Unger "are substantially devoid of liquid in the interior thereof" (col. 10,

line 65, to col. 11, line1); the vesicles of the presently claimed methods contain an aqueous medium.

In view of the above, particularly because the interior of Unger's liposomes is gas-filled and substantially devoid of liquid, Unger teaches away from the presently claimed methods. A reference that teaches away can defeat a finding of obviousness. *Winner Int'l Royalty Corp. v. Wang*, 202 F.3d 1340, 1349-1350 (Fed. Cir. 2000). Accordingly, Unger cannot be relied on for obviousness.

As stated above and set forth in the office action, neither Lichtenberger, Ghyczy nor Hayward discloses the use of stabilizers. Accordingly, neither Lichtenberger, Ghyczy nor Hayward renders the present claims obvious.

In light of the above, the pending claims are not obvious over the cited references, either alone or in combination. Therefore, it is believed that the present § 103(a) rejections have been overcome and should be withdrawn.

Conclusion

It is respectfully requested that the Examiner enter the present amendment in light of the foregoing remarks, and it is believed that all the claims are in condition for allowance. If the Examiner believes that a telephone interview would help expedite the successful prosecution of the claims, the undersigned attorney would be grateful for the opportunity to discuss any issues.

Please charge any payments due to Wilmer Cutler Pickering Hale and Dorr LLP Deposit Account No. 08-0219.

Respectfully submitted,
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Date: July 12, 2007

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